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18-Deoxy-13β,14-dihydrolycoctam: the lycoctamone rearrangement confirmed

Michael Benn,[a] Masood Parvez[a]* and Oliver Edward Edwards[b]

[a]Department of Chemistry, University of Calgary, 2500 University Drive NW, Calgary, Alberta, Canada T2N 1N4, and [b]678 Portage Ave., Ottawa, Ontario, Canada K1G 1T4
Correspondence e-mail: parvez@ucalgary.ca

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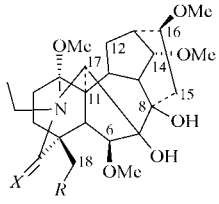
The structure of the title compound, $C_{23}H_{35}NO_4$, contains a unique pentacyclic ring system wherein one cyclohexyl ring adopts a chair conformation, two cyclohexyl rings are in boat conformations, and a six-membered heterocyclic ring and a cyclopentyl ring are in envelope conformations. The structures of the lycoctamones, α,β-unsaturated aldehydes produced by acid-catalyzed degradation of lactams of lycoctonine-type alkaloids, previously deduced from the results of extensive chemical investigations have been proven to be correct by the determination of the crystal structure of this compound.

Comment

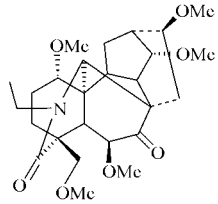
During early work on the structure of the norditerpenoid alkaloid lycoctonine, (1), it was discovered that the action of strong acids on the lactam derivative, (2), induced the loss of two methanol units and its transformation into a product named lycoctamone (Edwards *et al.*, 1954). Later studies revealed that lycoctamone was actually an α,β-unsaturated aldehyde, and extensive investigations of this compound and some congeners resulted in the proposed structure (3) (Benn *et al.*, 1971). As shown here, this structure incorporates a revision of the stereochemistry at C-1 required (Pelletier *et al.*, 1981; Edwards & Przybylska, 1982) as a result of an error in the original assignment in the X-ray crystallography of the derivative of (1) that had established the skeleton of these alkaloids (Przybylska & Marion, 1954; Przybylska, 1961); the same correction needs to be made to all other structures reported by Benn *et al.* (1971). The absolute structure of the lycoctonine series of compounds has been established previously (Przybylska & Marion, 1959).

The remarkable reorganization needed to produce (3) from (2) was rationalized as proceeding *via* a cascade of reactions, *viz.* a pinacolic rearrangement of (2) to (4), followed by a ring contraction of the protonated ketone *via* another acid-catalyzed 1,2-alkyl shift of the C-8,9 bond, to generate a carbocation that underwent a retro-Prins reaction with ring cleavage and loss of methanol, forming an aldehyde, which finally underwent an acid-catalyzed 1,2-elimination of another molecule of methanol. An alternative structure, (5), which would result from a fragmentation of protonated (4) induced by migration of the C-8,17 bond to generate a C-8 carbocation, appeared to be improbable because under the reaction conditions its exocyclic double bond would be expected to migrate to form a conjugated dienal system (Benn *et al.*, 1971).

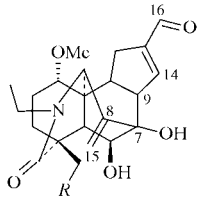
We now report the result of an X-ray crystallographic study which establishes the carbon skeleton of the lycoctamone system and confirms the conclusions reached from the chemical investigations.



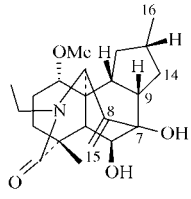
(1) R=OH X=CH_2
(2) R=OH X=O
(7) R=H X=O



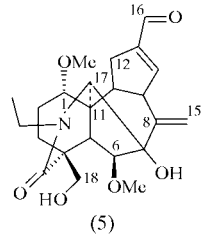
(4)



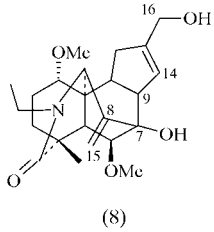
(3) R=OH
(6) R=H



(9)



(5)



(8)

Sodium borohydride reduction of 18-deoxylycoctamone, (6), prepared from 18-deoxylycoctonam, (7) (Benn *et al.*, 1971), gave the corresponding allylic alcohol (8), which was then subjected to hydrogenation over palladium, a process known to result in hydrogenolysis as well as reduction of the endocyclic double bond (Edwards *et al.*, 1954; Benn *et al.*, 1971), to afford in good yield 18-deoxy-13β,14-dihydrolycoctam, (9), as a crystalline product. X-ray crystallography of this established the structure reported in this paper. This confirmed the molecular skeleton as that of (3), and not (5), and additionally showed that as expected hydrogenation had occurred from the β-face. Thus, the structures assigned to lycoctamone and its analogues have been confirmed.

Selected geometric parameters of (9) are given in Table 1. The structure contains a unique pentacyclic ring system (Fig. 1)

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that has not been reported in any structure contained in the latest version of Cambridge Structural Database (2006 Release; Allen, 2002). The six-membered rings C1–C5/C11 (ring *A*), C5–C7/C9–C11 (ring *B*), C7–C11/C17 (ring *C*) and C4/C5/C11/C17/C19/N1 (ring *D*) adopt chair, boat, boat and C11-envelope conformations, respectively. The five-membered ring, C9/C10/C12–C14 (ring *E*), exhibits a C13-envelope conformation. The puckering parameters (Cremer & Pople, 1975) for ring *A* are Q = 0.562 (4) Å, θ = 167.7 (4)° and φ = 8(2)°. In ring *B*, atoms C7 and C11 lie 0.735 (5) and 0.709 (5) Å, respectively, out of the plane formed by the remaining four atoms of the ring, the maximum deviation of any of these fours atoms from the plane being 0.052 (2) Å. Similarly, in ring *C*, atoms C7 and C11 lie 0.735 (5) and 0.709 (5) Å, respectively, out of the plane formed by the remaining four atoms of the ring, with a maximum deviation of 0.082 (2) Å. In the heterocyclic ring *D*, atom C11 lies 0.720 (5) Å out of the plane formed by the remaining five atoms, which show large deviations from planarity [between 0.120 (2) and 0.146 (3) Å].

The molecular dimensions in (9) are as expected and the structure is stabilized by strong intermolecular O—H···O hydrogen bonds (Table 2), linking the molecules into spirals along the *b* direction.

Experimental

NMR spectra were recorded of samples dissolved in $CDCl_3$ (^{1}H at 400 MHz, with residual $CHCl_3$ as reference, δ_H 7.25 p.p.m.; ^{13}C at 100 MHz, with the center line of the solvent resonance as reference, δ_C 77.0 p.p.m.) and EIMS were measured using 70 eV sample bombardment. 18-Deoxylycoctamol, (8): m.p. 500–505 K (from Me_2CO–hexanes); EIMS *m*/*z* 403.2352, $C_{23}H_{33}NO_5$ requires 403.2359; ^{1}H NMR: δ_H 5.38 (1H, *br s*, H-14), 5.12 (1H, *br s*, H-15*A*) and 5.14 (1H, *br s*, H-15*B*), 4.19 (1H, *d*, *J* = 2 Hz, H-17), 4.13 (2H, *br s*, H-16), 3.93 (1H, *dq*, *J* = 14.1 and 7.1 Hz, H-20*A*), 3.57 (3H, *s*, OCH_3), 3.38 (1H, *br m*), 3.30 (3H, *s*, OCH_3), 3.21 (1H, *d*, *J* = 4.1 Hz, H-6), 3.07 (1H, *br m*), 2.97 (1H, *dq*, *J* = 14.1 and 7.1 Hz, H-20*B*), 2.39 (3H, *m*), 1.99 (1H, *m*), 1.94 (1H, *m*), 1.58 (1H, *dd*, *J* = 4.1 and 2.1 Hz, H-5), 1.31 (2H, *m*), 1.27 (3H, *s*, H-18), and 1.12 (3H, *t*, *J* = 7.1 Hz, H-21); ^{13}C NMR: δ_C 172.6 (*s*), 149.1 (*s*), 143.9 (*s*), 121.5 (*d*), 113.0 (*t*), 85.4 (*d*), 83.3 (*d*), 61.7 (*t*), 60.3 (*q*), 56.9 (*d*), 56.5 (*q*), 53.2 (*d*), 47.7 (*d*), 39.0 (*t*), 36.3 (*t*), 36.0 (*t*), 25.2 (*t*), 22.2 (*q*), and 11.7 (*q*). 18-Deoxy-13β,14-dihydrolycoctam, (9): m.p. 484–486 K (from Me_2CO–hexanes); EIMS *m*/*z* 389.2565, $C_{23}H_{35}NO_4$ requires 389.2566; ^{1}H NMR: δ_H 5.27 (1H, *br s*, H-15*A*), 5.25 (1H, *br s*, H-15*B*), 4.08 (1H, *d*, *J* = 1.5 Hz, H-17), 3.99 (1H, *dq*, H-20*A*), 3.55 (3H, *s*, OCH_3), 3.28 (3H, *s*, OCH_3), 3.22 (1H, *d*, *J* = 4 Hz, H-6), 3.01 (1H, *m*), 2.99 (1H, *dq*, H-20*B*), 2.76 (1H, *m*), 2.1–1.8 (4H, *m*), 1.75–1.55 (4H, *m*), 1.49 (1H, *dd*, *J* = 1.5 and 4 Hz, H-5), 1.26 (3H, *s*, H-18), 1.13 (3H, *t*, *J* = 7.1 Hz, H-21), 0.96 (3H, *d*, *J* = 6 Hz, H-15), and 0.94 (1H, *m*); ^{13}C NMR: δ_C 172.7 (*s*), 144.1 (*s*), 112.9 (*t*), 84.5 (*d*), 83.5 (*d*), 78.4 (*s*), 60.2 (*q*), 56.3 (*d*), 56.2 (*q*), 54.1 (*d*), 50.9 (*q*), 42.8 (*s*), 39.2 (*t*), 39.1 (*d*), 38.6 (*t*), 38.5 (*s*), 36.5 (*t*), 34.6 (*d*), 33.3 (*t*), 25.4 (*t*), 22.1 (*q*), 18.8 (*q*), and 11.7 (*q*).

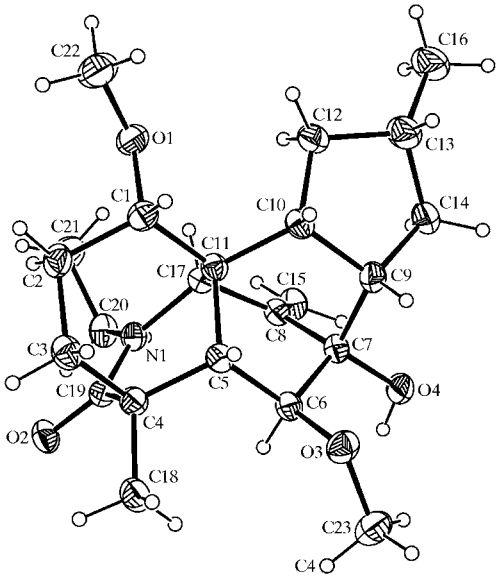

Figure 1
An *ORTEPII* (Johnson, 1976) drawing of (9), showing the crystallographic numbering scheme. Displacement ellipsoids have been plotted at the 25% probability level.

Crystal data

$C_{23}H_{35}NO_4$	Z = 2
M_r = 389.52	D_x = 1.244 Mg m^{-3}
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
a = 9.675 (5) Å	μ = 0.08 mm^{-1}
b = 10.401 (6) Å	T = 295 (2) K
c = 11.063 (7) Å	Needle, colorless
β = 110.86 (3)°	0.12 × 0.04 × 0.03 mm
V = 1040.3 (10) Å^3	

Data collection

Nonius KappaCCD diffractometer	4396 measured reflections
ω and φ scans	2486 independent reflections
Absorption correction: multi-scan (*SORTAV*; Blessing, 1997)	1390 reflections with $I > 2\sigma(I)$
T_{min} = 0.990, T_{max} = 0.997	R_{int} = 0.060
	θ_{max} = 27.5°

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.057P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.051	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.124	$\Delta\rho_{max}$ = 0.17 e Å^{-3}
S = 1.01	$\Delta\rho_{min}$ = −0.20 e Å^{-3}
2486 reflections	Extinction correction: *SHELXL97*
255 parameters	Extinction coefficient: 0.048 (8)
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

O1—C22	1.419 (6)	O4—C7	1.420 (4)
O1—C1	1.434 (4)	N1—C19	1.350 (4)
O2—C19	1.238 (4)	N1—C20	1.466 (4)
O3—C23	1.420 (5)	N1—C17	1.497 (5)
O3—C6	1.432 (4)		
C22—O1—C1	113.1 (3)	C19—N1—C17	125.5 (3)
C23—O3—C6	115.4 (3)	C20—N1—C17	115.7 (3)
C19—N1—C20	118.8 (3)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O4—H4···O2^{i}	0.82	2.08	2.900 (4)	177

Symmetry code: (i) $-x+1, y-\frac{1}{2}, -z$.

The H atoms were located in difference Fourier syntheses and were included in the refinements at idealized positions (C—H = 0.96 Å) with isotropic displacement parameters equal to 1.5 (hydroxy

atom) and 1.2 (the rest) times the equivalent displacement parameters of the atoms to which they are bonded. The final difference map was free of any chemically significant features. An absolute structure was not established in this analysis; Friedel pairs of reflections were merged.

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997); data reduction: *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SAPI91* (Fan, 1991); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

The initial studies were carried out at the National Research Council, Ottawa; the X-ray studies were personally funded by MB.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG3014). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Benn, M. H., Connolly, J. D., Edwards, O. E. & Stojanac, Z. (1971). *Can. J. Chem.* **49**, 425–438.
Blessing, R. H. (1997). *J. Appl. Cryst.* **30**, 421–426.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Edwards, O. E., Marion, L. & MacIvor, R. A. (1954). *Can. J. Chem.* **32**, 708–717.
Edwards, O. E. & Przybylska, M. (1982). *Can. J. Chem.* **60**, 2661–2667.
Fan, H. F. (1991). *SAPI91*. Rigaku Corporation, Tokyo, Japan.
Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Nonius (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.
Otwinowski, Z. & Minor, W. (1997). *Methods in Ezymology*, Vol. 276, Macromolecular Crystallography, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Pelletier, S. W., Mody, N. V., Varughese, K. I., Maddry, J. A. & Desai, H. K. (1981). *J. Am. Chem. Soc.* **103**, 6536–6538.
Przybylska, M. (1961). *Acta Cryst.* **14**, 424–429.
Przybylska, M. & Marion, L. (1954). *Can. J. Chem.* **34**, 185–187.
Przybylska, M. & Marion, L. (1959). *Can. J. Chem.* **37**, 1843–1845.
Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.